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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/716,924	11/19/2003	Colin Louis Masters	9287ZYA	6426

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 10/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/716,924	MASTERS ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-27,37-39,43 and 44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-27,37-39,43 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Formal matters

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Response to Amendment

2. Claims 25, 37 have been amended, claims 43 and 44 have been added and claims 28-36 and 40-42 have been canceled as requested in the amendment filed on September 12, 2005. Following the amendment, claims 25-27, 37-39 and 43-44 are pending in the instant application.

Claims 25-27, 37-39 and 43-44 are under examination in the instant office action.

3. The Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Any objection or rejection of record, which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

5. Applicant's arguments filed on September 12, 2005 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections - 35 USC § 112

6. Claims 25-27, 37-39 and 43-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement for reasons of record as applied to claims 25-42 in section 3 of Paper mailed on June 13, 2005.

Applicant traverses the rejection on the premises that the "unique recognition of the present invention [is] that by modulating the levels of divalent cations (particularly zinc) or heparin, the range, type and/or extent of APP cleavage can be altered" (top at page 10 of the Response). Applicant further refers to the Declaration of Dr. Cappai, which discloses that zinc chelators are capable to cross the blood brain barrier and also provides additional new data regarding zinc-binding and APP processing. Applicant's arguments have been fully considered but are not deemed to be persuasive for the following reasons.

With respect to analysis of one of the *Wands* factors, such as the state of the prior art, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what was known and disclosed in the art at the time invention. The analysis of the state of the prior art, when evaluating the enablement of the claims, allows establishing the predictability or unpredictability of that specific art. Therefore, while it is true that "the deficiency of the prior art relating to the role of zinc does not warrant a conclusion of non-enablement" (top at page 10 of the Response), in view of the novelty of the instant invention, one skilled in the art would have to solely rely on the instant disclosure in order to practice the instant invention as currently claimed. However, the limited information presented in the instant specification clearly is not sufficient for a worker of skill in the art to practice the claimed method with reasonable expectation of success.

The art of treatment of Alzheimer's disease is generally considered unpredictable, as there is no known cure or efficient treatment available. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970), the court held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while

unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved" (emphasis added).

The standard of an enabling disclosure is not the ability to make and test if the invention worked but one of the ability to make and use with a reasonable expectation of success. In the instant case, in view of the total absence of the prior art data supporting Applicant's hypothesis regarding the beneficial effects of decreasing levels of circulating zinc to treat Alzheimer's disease and further in view of the art at the time of invention that describes opposite effects (improvement symptoms of Alzheimer's disease by using zinc supplements, see article of Constantinidis of the previous office action of record), a skilled practitioner would have to engage in a significant amount of undue research and experimentation to discover how to practice the claimed method.

The Declaration of Cappai under 37 CFR 1.132 filed on Sept 29, 2005 is insufficient to overcome the rejection of claims 25-27, 37-39 and 43-44 based upon 35 USC 112, first paragraph as set forth in the last Office action for the following reasons.

The Declaration discloses that chelators of zinc were known at the time of the filing of the instant application (section 9). The Declaration further states that at the time of invention it could be easily determined if a compound (a zinc chelator) could cross the blood brain barrier (section 10). There is no disagreement with these statements.

In sections 7 and 12-13, Dr. Cappai refers to additional experiments that were performed to show the effects of zinc binding on APP processing. Applicant is reminded that in order to satisfy the enablement requirement under 35 USC 112, first paragraph, the invention must be enabled at the time of filing, which precludes any reliance on data obtained during further research and experimentation. However, in the instant case, it appears that the additional data disclosed in the Cappai Declaration pertains only to APP processing. The importance of processing of APP in etiology of Alzheimer's disease is not disputed. However, there is no evidence of record to show that reduction of Aβ40 levels within *in vitro* system using genetically modified CHO (Chinese Hamster Ovary) cells when treated with zinc-binding agents is predictive of successful treatment of Alzheimer's disease. As fully explained in the previous office action, Alzheimer's disease is a complex neurodegenerative pathology and is not solely attributed to the amount of produced Aβ40.

Thus, the evidence of record, which is limited to originally disclosed *in vitro* experiments of zinc, heparin and APP binding and Examples 3 and 6 disclosing worsening conditions of two Alzheimer's disease patients receiving zinc supplements, is inadequate to support a conclusion

that administration of zinc-binding agent could affect *in vivo* APP processing in a way that it would lead to treatment of Alzheimer's disease.

In view of the lack of teachings and unpredictability of the art set forth earlier, and also the total absence of the working examples, the instant specification is not found to be enabling for a method for treating Alzheimer's disease. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use Applicants' invention as currently claimed.

7. Claim 37 stands rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for reasons of record in section 7 of Paper mailed on June 13, 2005. Applicant argues that "[i]t is clear from the language of claim 37 that the amount of agent is effective for modulating the interaction within the central nervous system" (middle at page 8 of the Response). The Examiner maintains the position that the recitation of "an effective amount" is vague and ambiguous without an objective as what the amount is effective for. Nothing in the claim language points out that the effective amount of the zinc-binding agent is effective to achieve the modulation of the interaction and not effective for reduction of abnormal processing of APP, for example.

New grounds of rejection necessitated by amendment

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 25-27, 37-39 and 43-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 25 and 37, as amended, are vague and indefinite because the relationship between "a zinc-binding agent" and "a divalent or trivalent cation" is not clear. It appears that the claims require modulation of interaction of a zinc-binding agent and any divalent or trivalent cation, which raises additional issues with respect to enablement of the instant invention. Clarification is required.

11. Claims 26-27, 38-39 and 43-44 are indefinite for being dependent from indefinite claims.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (571) 272-0870. The examiner can normally be reached on 8:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Olga N. Chernyshev, Ph.D.
Primary Examiner
Art Unit 1649

October 07, 2005